

BB-907
TAR-3135

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: January 5, 1982
SUBJECT: EPA Registration Number: 5204-1
Biomet TBTO

003135

FROM: Deloris F. Graham *DFG 1/8/82*
FHB/TSS *E 1/8/82*
TO: Henry Jacoby
Product Manager (21)

Applicant: M&T Chemicals, Inc.
P.O. Box 1104
Rahway, NJ 07065

Active Ingredient:

Bis(tri-n-butyltin)oxide.....95%
Inert Ingredient..... 5%

Background: Submitted two Acute Oral Studies. These studies conducted by Bio/dynamics, Inc. Data under accession number 246070.

Recommendations:

1. FHB/TSS finds these data acceptable to support conditional registration of the product on which tested.

Review:

1. Acute Oral Toxicity Study on BioMet TBTO: Bio/dynamics, Inc.; Project #6656-81; September 29, 1981.

Procedure: 5 groups consisting of 5M and 5F rats each received one of the following doses per group: 100, 143, 204, 292 and 416 mg/kg. Observations were made at 1, 2, and 4 hours after dosing and daily thereafter for 14 days. Necropsy performed on all animals.

Results: At 100 mg/kg, 1/5 M and 1/5 F died; at 143 mg/kg, 1/5 M and 5/5 F died; at 204 mg/kg, 3/5 M and 4/5 F died; at 292 mg/kg, 4/5 M and 5/5 F died; at 416 mg/kg, 5/5 M and 5/5 F died.

Toxicologic signs observed included ataxia; hypopnea; hypoactivity; wet rales; nasal, oral or ocular discharge; soft stool; fecal and urinary staining; hypothermia; prostration; decreased food consumption; emaciation; an unthrifty coat; ulceration; alopecia of the skin of the ano-genital area; partially closed eye lids which were considered indicative of a spontaneous viral infection (sialodacryoadentitis).

Necropsy revealed lungs: red/dark foci, mottled, bright red and pale red; liver: normal post mortem changes, mottled dark red edges; stomach: contained colored fluid and/or suspension or solid red foci, thick/thin walls, mottled walls, distended with gas, hair; small intestines: contained colored fluid and/or suspension or solid mottled walls, purple walls, normal post-mortem changes, distended with gas, thin walls; large

1073

intestines: contained colored fluid and/or suspension or solid mottled walls, red walls, distended with gas, thin walls; spleen: small, dark red, mesentery adhered; adrenals: large, red foci, pale red/red/dark red, mottled, dark purple, small; ovaries, orange, cysts; uterus: distended with clear fluid; testes: (right and/or left) in body cavity, left testes absent.

LD₅₀ for males was 193 mg/kg with 95% confidence limits between 136 and 250 mg/kg. LD₅₀ for females was 123 mg/kg with 95% confidence limits between 97 and 149 mg/kg. Combined LD₅₀ for males and females was 150 mg/kg with 95% confidence limits between 124 and 176 mg/kg.

Study Classification: Core Guideline Data.

Toxicity Category: II - WARNING

2. Acute Oral Toxicity Study on TBTO (Alkyl-sourced): Bio/dynamics, Inc.; Project #6657-81; September 28, 1981.

Procedure: Procedures same as number one except doses used were 70, 100, 143, 204 and 292 mg/kg.

Results: At 70 mg/kg, 1/5 F died; at 100 mg, 1/5 F died; at 143 mg/kg, 1/5 M and 2/5 F died; at 204 mg/kg, 4/5 M and 5/5 F died; at 292 mg/kg, 4/5 M and 5/5 F died.

Toxicologic signs included ataxia, hypopnea; hypoactivity; wet and/or dry rales; nasal, oral or ocular discharge; soft stool; fecal and urinary staining; hypothermia; prostration and tremors seen prior to death in a few animals; decreased food consumption; emaciation; and unthrifty coat; ulceration and alopecia of the skin of the ano-genital area. Some of the animals exhibited partially closed eyelids and alopecia around the neck; this was considered indicative of a spontaneous viral infection (sialodacryoadentitis) and not an effect of test material.

Necropsy revealed lungs: mottled, red foci, pale red, bright red, pitted; liver: accentuated lobular pattern, post-mortem changes; stomach: contained colored fluid and/or suspension, mottled walls, thick walls, red foci; small intestines: contained colored fluid and/or suspension, distended, mottled; large intestines: contained colored fluid and/or suspension, mottled; spleen small; kidneys: hollow; adrenals: red, pale red/dark red, red foci, patches, large, mottled; uterus: post-mortem changes (gray); testes: (right and/or left) in body cavity, white fibrous substance.

LD₅₀ for males was 180 mg/kg with 95% confidence limits between 130 and 230. LD₅₀ for females was 150 mg/kg with 95% confidence limits between 130 to 170. Combined LD₅₀ for males and females was 170 mg/kg with 95% confidence limits between 142 and 192 mg/kg.

Study Classification: Core Guideline Data.

Toxicity Category: II - WARNING

2

TBTO Scientific Reviews

Page 3 is not included in this copy.

Pages _____ through _____ are not included in this copy.

The material not included contains the following type of information:

- ☐ Identity of product inert ingredients
 - ☐ Identity of product impurities
 - ☐ Description of the product manufacturing process
 - ☐ Description of product quality control procedures
 - ☐ Identity of the source of product ingredients
 - ☐ Sales or other commercial/financial information
 - ☒ A draft product label
 - ☐ The product confidential statement of formula
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